improvement of nasal breathing in mammals, said method comprising a step of administering to a subject in need thereof a liquid or a solid composition consisting essentially of from about 0.01 to about 20% an alkylaryl polyether alcohol polymer nasally or pharyngeally.

2. (Amended) The method of claim 1, wherein said composition is applied from antegrade or from retrograde.

4. (Amended) The method of claim 3 wherein the composition is formulated as a nasal or pharyngeal spray, as a nasal solution, as a dry powder, as a lozenge or as a nasal aerosol.

5. (Amended) The method of claim 4 useful for treatment and prevention of snoring in humans comprising administration of the composition consisting of from about 0.2 to about 20% of tyloxapol.

6. (Amended) The method of claim 5 wherein the composition is consisting of from about 1 to about 10% of tyloxapol.

7. (Amended) The method of claim 6 wherein the composition is formulated as the nasal or pharyngeal spray.

8. (Amended) The method of claim 7 wherein the composition is consisting of about 1% of tyloxapol.

9. (Amended) The method of claim 4 useful for treatment and prevention of sleep apnea in humans comprising administration of the composition consisting of from about 0.5 to about 20% of tyloxapol.

10. (Amended) The method of claim 9 wherein the composition is consisting of from about 5 to about 15% of tyloxapol.

11. (Amended) The method of claim 10 wherein the composition is formulated as the nasal or pharyngeal spray.

12. (Amended) The method of claim 11 wherein the composition is consisting of about 5% of tyloxapol.

Sub C1 cont.

13. (Amended) The method of claim 4 useful for treatment and prevention of sudden infant death syndrome in infants comprising administration of the composition consisting of from about 0.01 to about 5% of tyloxapol.

A2 cont

14. (Amended) The method of claim 13 wherein the composition is consisting of from about 0.1 to about 2% of tyloxapol.

15. (Amended) The method of claim 14 wherein the composition is formulated as the nasal spray or nasal solution.

16. (Amended) The method of claim 15 wherein the composition consisting of about 0.1% of tyloxapol is administered to an infant before sleep in 1-3 drops.

17. (Amended) The method of claim 4 useful for improvement of nasal breathing in humans comprising administration of the composition consisting of from about 0.2 to about 20% of tyloxapol.

18. (Amended) The method of claim 17 useful for improvement of nasal breathing during physical activity or for improvement of nasal breathing impaired due to a disease, infection or surgery by administering to a subject in need of such treatment the composition consisting of from about 0.5 to about 10% of tyloxapol.

19. (Amended) The method of claim 18 wherein the physical activity is diving, mountain hiking, high altitude mountain climbing or flying and wherein the composition is formulated as the nasal or pharyngeal spray or lozenge.

20. (Amended) The method of claim 19 wherein the composition consisting of about 1% of tyloxapol is formulated as nasal drops, spray or lozenge.

22. (Amended) The method of claim 21 wherein the treatment for improvement of nasal breathing in animals comprises administration of the nasal spray composition consisting of from about 0.2 to about 20% of tyloxapol.

23. (Amended) The method of claim 22 wherein the composition is consisting of from about 5 to about 15% of tyloxapol.

24. (Amended) The method of claim 1 wherein the composition consisting of from about 1% to about 10% of the alkylaryl polyether alcohol polymer, additionally comprises 50 mg glycerol, and 20 mg sodium bicarbonate dissolved in an aqueous solution or in normal or diluted saline.

25. (Amended) A device for administration of a nasal or pharyngeal composition consisting essentially of from about 0.01 to 20% of alkylaryl polyether alcohol polymer suitable for treatment and prevention of snoring, sleep apnea, sudden infant death syndrome or for improvement of nasal breathing.

28. (Amended) The device of claim 26, wherein the device is a spray container suitable for administration of the composition to a nasal or upper pharyngeal mucosa using an extension nozzle.

29. (Amended) The device of claim 28 wherein the composition is formulated as a dry powder and the device is the dry powder inhaler.

30. (Amended) A nasal or pharyngeal composition for treatment or prevention of snoring, sleep apnea, sudden infant death syndrome and improvement of nasal breathing in mammals, consisting essentially of from about 0.1 mg to about 200 mg of an alkylaryl polyether alcohol polymer alone or in combination with another alkylaryl polyether alcohol polymer, in admixture with a pharmaceutically acceptable excipient or additive.

32. (Amended) The composition of claim 31 wherein tyloxapol is present in concentration from about 1 mg to about 100 mg dissolved in normal or diluted saline.

REMARKS

This Amendment and Remarks are filed in response to the First Office Action dated May 7, 2002 where all claims stand rejected under 35 U.S.C. 102 (b).

Rejections under 35 U.S.C. 102(b)

Claims 1-36 are rejected under 35 U.S.C. 102 (b) as being anticipated by Meyer et al (US Patent 5,958,902). Examiner also cites reference Clements (US Patent 4,826,821) which is incorporated by reference by Meyer.

Examiner argues that Meyer relates to the application of a lung surfactant to the posterior pharyngeal region prior to sleep to significantly reduce episodes of sleep disturbance resulting in apnea and teaches that sleep apnea has been associated with sudden death (col.1, lines 46-50). The invention may provide the lung surfactant in a convenient applicator container for easy use and storage (Abstract).

Examiner further argues that the lung surfactant can be any of those commercially available and licensed by the FDA, including artificially compounded compositions such as Exosurf® which contains phospholipids and a preferred surface active agent, tyloxapol (col. 4, lines 50-54) and also that Meyer teaches that U.S. Patent 4,826,821, by Clements, incorporated by Meyer by reference, teaches using synthetic surfactant compositions containing tyloxapol. Specifically, Examiner argues that U.S. Patent 4,826,821 teaches that surface active agents such as tyloxapol can be present in the compositions from 6-11% ('821, col 6, lines 56-65).

Finally, Examiner argues that during application of the invention of Meyer, a pressurized aerosol can, a squeeze bottle, or a pump bottle may be used. The surfactant will typically be applied through the oral cavity, but it may be delivered nasally when the subject is supine (col 5, lines 44-50).

Applicant disagrees. Applicant's invention is not anticipated by Meyer ('902) or by Clements ('821). Anticipation requires that the invention is patented or described in a printed publication or is in public use or on sale in this country. That is clearly not the case here as neither Meyer or Clements describe the use of the alkylaryl polyether alcohol polymer compound alone for use as described herein. At most they describe compositions which contain tyloxapol, one of the alkylaryl compounds as a component of such compositions.

However, to meet Examiner's rejection and to make claims clearly directed only to his invention, Applicant amended claims 1, 25 and 30 to be limited to, that is "consisting essentially of" from 0.01 to 20% of alkylaryl polyether alcohol polymer. While the above cited references may have but do not really need the presence of tyloxapol, the current invention needs and must contain at least one alkyaryl polyether alcohol polymer in amounts stated. The language "consisting essentially of" clearly defines the bounds and

metes of the current invention.

This amendment thus removes all grounds for rejections advanced by the Examiner. Distinguishing features of the current invention from the cited prior art are as follows:

The invention provides a method, device and a composition for treatment and prevention of snoring, sleep apnea, sudden infant death and improvement of nasal breathing in mammals. The method is based on administration of a composition consisting of from about 0.01 to about 20% of alkylaryl polyether alcohol polymer nasally or pharyngeally, depending on the conditions to be treated and on the regimen to be used for such treatment.

This is clearly different from both '902 and '821 patents as no other therapeutic agents are needed or required for practicing the current invention.

'902 patent describes a method and composition for treating sleep apnea by administering a composition containing a synthetic or naturally occurring pulmonary alveolar surfactant of which the primary component is a phospholipid.

The surfactant may be any naturally occurring or artificially compounded composition commercially available and approved for treating infant respiratory distress syndrome ('902, col 4, lines 2-6). Commercially available surfactants are listed in Table 1, col. 4. One of the listed surfactants, known under the name of Exosurf® contains a small amount of tyloxapol in combination with a phospholipid dipalmitoyl phosphatidyl choline and cetyl alcohol (Table 1, lines 24-27). Specifically, Exosurf® contains 13.5 mg/ml of phosholipid (dipalmitoyl phosphatidyl choline), 1.5 mg/ml of cetyl alcohol and 1 mg/ml of tyloxapol. For exact formulation of Exosurf® please see enclosed page 1380 from Physician's Desk Reference, 55th Edition 2001 (enclosed).

The composition disclosed by Meyer consists <u>essentially</u> of dipalmitoyl phosphatidyl choline, a C14-C18 fatty alcohol and a nonionic surface active agent tyloxapol ('902, col 4, lines 50-54)

in amounts given above.

'902 further states (col 4, lines 62-67; col 5, line 1) that the use of any of these phospholipids in purified form in low percentage amounts of about 0.5 to about 15 percent (v/w), in combination with the major surfactant component, dipalmitoyl phosphatidyl choline (about 28-53%, w/w) with or without adding surfactant associated proteins (SP-A, SP-B or SP-C) is a synthetic form of surfactant which is applicable to their invention.

'902 also states that any combination of the above ingredients will have efficacy so long as the tissue coating and adhesive properties of natural surfactant are mimicked, and there is an effective lowering of surface tension of the film to 10 millinewtons or less (col 5, lines 11-17).

Definition of the natural surfactant is found in '821 patent, col 2, lines 21-32. There the natural surfactant is described as a complex mixture of many components, the major component of which is a lipid, dipalmitoyl phosphatidyl choline (1,2 dipalmitoyl-sn-3-glycerophosphoryl choline). Dipalmitoyl phosphatidyl choline commonly abbreviated as DPPC, occurs in lung surfactant to the extent of about 41% by weight. Mixed lecithins make up about 25% by weight; cholesterol makes up about 9% by weight; mixed proteins about 9% by weight; phosphatidyl ethanolamine, about 5%; various glycerides and phosphatidyl serine and phosphatidyl glycerol, about 4%, respectively; lysolecithin, about 2%; with sphingomyelin and fatty acids, each making up about 1%. In any case, both bovine and human lung surfactant comprise at least 40% of dipalmitoyl phosphatidyl choline ('821, col 2, lines 35-38).

Examiner relies on the reference Clements ('821) and the synthetic surfactant composition disclosed therein of which definition is cited immediately above. '821 patent describes compositions useful in alleviating the symptoms of mammalian respiratory distress syndrome. Such compositions essentially consist of three components, namely, dipalmitoyl phosphatidyl

choline, a fatty alcohol, such as hexadecanol, and a compound serving as a surface active agent, specifically a nonionic polymer of the alkylaryl polyether alcohol. That surface active agent may be tyloxapol ('821, col 4, lines 21-28 and col 6, lines 51-52). There is no description of composition which would contain alkylaryl polyether alcohol alone without other components.

Thus neither of the '902 or '821 references utilizes alkylaryl polyether alcohol polymer alone for treatment of snoring, sleep apnea, sudden infant syndrome or improvement of breathing.

Both references utilize lung surfactant compositions which essentially contain very large percentages (up to 90%) of a phospholipid in combination with other compounds, such as fatty alcohols or acids. Surface active agents, such as tyloxapol, may be added to these compositions and are thus present in small or minute amounts. They are not essential to the inventions described in these two references.

Applicant amended claims to read "consisting essentially of" rather than "comprising" thereby eliminating any possibility of needing to have any phospholipid, such as dipalmitoyl phosphatidyl choline present in the composition. All that is essential for the current composition is the presence of at least one of the alkylaryl polyether alcohol polymers.

Applicant's invention is based on the findings that tyloxapol or another alkylaryl polyether alcohol polymer, alone, in an aqueous solution such as saline, preferably half or quarter diluted saline, provides effective protection against and treatment of snoring and sleep apnea, improves sleep pattern and breathing and prevents infant sudden death syndrome. Utilized amount is typically very low and as little as 0.1% tyloxapol was shown to already have preventive effect on snoring and improving apnea. The current composition is simple, can be administered through mouth or nose, is safe and practical.

As stated above, anticipation under 35 U.S.C. 102 (b) requires that the anticipated invention be patented or described in a printed publication in this or a foreign country, Applicant respectfully submits that the current invention has not been so described and is thus not anticipated.

Withdrawal of the rejections against current claims is respectfully requested and Notice of Allowance is solicited.

SUMMARY

In summary, Applicant substantially amended claims and describes distinguishing features and provides arguments showing that the current invention is not anticipated from the cited prior art. It is believed that with this amendment, all claims are in conditions for immediate allowance. Notice of allowance is respectfully requested.

Should Examiner require minor amendments to the claims necessary for allowance, Applicant encourages Examiner to call undersigned at 650-324-1677.

Respectfully submitted,

Date: July 22, 2002

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